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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,444	07/21/2004	Helenius Jan Kloosterboer	O-2002.713 US	4004

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,444	KLOOSTERBOER ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 6/26/2006. Claim(s) 7-13 are pending and examined herein. Applicant's arguments have been fully considered but found not persuasive. The 103(a) rejection is maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 7-13 are rejected under 35 U.S.C. 103(a) as being obvious over Deckers et al. (EP 0 613 687 A1) in view of Huebner et al. (US Patent 6,262,098 B1) and further in view of Sas et al. (EP 0 389 035 A1).

The instant claims are directed to a method of treating the estrogen-deficient related complaints in female patients that exhibit these complaints while the female patients are on treatment with a drug that prevents the synthesis of endogenous estrogen comprising administering to the female an effective amount of tibolone.

Deckers et al. teach a method of treating breast cancer with tibolone without undesirable side effects associated with estrogen (pg. 2, lines 6-41). The daily dosage for tibolone is 0.003 to 3.0 mg per kg body weight, which for the average individual weighing 70 kg is 0.21 to 210 mg daily dosage (pg. 2, lines 51-53).

However, Deckers et al. fail to disclose aromatase inhibitors and the estrogen-related complaints.

Huebner et al. teach that aromatase inhibitors, such as exemestane, aminogluethimide, letrozole, and anastrozole (col. 34, lines 24-45) can be used for treating estrogen receptor-mediated disorders including osteoporosis and breast cancer (col. 13, lines 38-50).

Sas et al. teach that tibolone (pg. 2, lines 5-15) is useful for treating menopausal complaints (climacteric) and osteoporosis (bone loss) (pg. 2, lines 51-52).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine the treatments of osteoporosis and breast cancer by administering tibolone during or after administration of aromatase inhibitors.

A person of ordinary skill in the art would have been motivated to administering tibolone during or after administration of aromatase inhibitors for the treatment of

osteoporosis and breast cancer because (1) both are taught to treat estrogen-deficient disorders such as osteoporosis; (2) both are taught to treat breast cancer; and (3) tibolone has the added benefit of reducing undesirable side effects, such as menopausal complaints, in treating estrogen-deficient disorders. A person of ordinary skill in the art would have been motivated to treat estrogen-deficient complaints in females with tibolone during or after administration of aromatase inhibitors because of the reasonable expectancy of successfully treating the disorder without the common side effects associated with estrogen-deficiency.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments

Applicant argues that Deckers and Heubner et al. does not disclose using tibolone to treat estrogen-deficient complaints in females being treated with a drug that prevents the synthesis of endogenous estrogen. Applicant also argues that there is no suggestion in Sas et al. to use tibolone with an aromatase inhibitor.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on

the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues impermissible hindsight that one skilled in the art would not consider that both aromatase inhibitors and tibolone could be used for the same purpose, i.e. to treat osteoporosis. Applicants also argue that one skilled in the art would not be motivated to select aromatase inhibitors out of a laundry list of compounds. This is not persuasive because Huebner et al. clearly teach that aromatase inhibitors can be used for osteoporosis and Sas et al. clearly teach that tibolone can be used to treat osteoporosis. A person of ordinary skill in the art would have been motivated to treat estrogen-deficient complaints in females with tibolone during or after administration of aromatase inhibitors because of the reasonable expectancy of successfully treating the disorder without the common side effects associated with estrogen-deficiency.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SHENGJUN WANG
PRIMARY EXAMINER